

REMARKS

Favorable reconsideration of this application is requested in view of the above amendments and the following remarks.

Claim 1 has been amended to limit the compounds to be deuterated to those having at least one carbon-carbon double bond or carbon-carbon triple bond, and the claim further amended editorially. Accordingly, claim 7 has been canceled without prejudice, and claims 13 and 17 have been amended editorially.

Claims 1-3, 5-9, 13-14 and 16-17 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection.

Claim 1 has been amended editorially, and claim 1 has no antecedent basis issue. Accordingly, this rejection should be withdrawn.

Claims 1-3, 5-9 and 11-17 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Kato et al. (U.S. Patent No. 4,874,890) in view of Sajiki et al. (Synlett, 2002, No. 7, 1149-1151), in further view of Garnett et al. (Aust. J. Chem, 1961, 14, 441-448) (Garnett I), and in further view of Garnett et al. (Journal of Catalysis, 1963, 2(4), 339-347) (Garnett II), and in further view of Kawai et al. (U.S. Patent No. 4,591,626). Applicants respectfully traverse this rejection.

Claim 1 is directed to a method for deuteration of a compound of formula [1] having at least one multiple bond, which is a carbon-carbon double bond or a triple bond. The method of claim 1 includes a step of reacting the compound under neutral condition with a deuterated solvent other than D₂O₂ in the co-presence of only one activated catalyst, where the catalyst is activated prior to performing the deuteration reaction. Claim 1 further recites that the at least one multiple bond is formed in the group of R¹ and/or R² in an aliphatic portion thereof, among other features. By using the catalyst activated prior to the deuteration reaction, the compound having one or more multiple bonds such as the carbon-carbon double bond and/or carbon-carbon triple bond can be deuterated at a significantly higher deuteration ratio than the compound deuterated with

an inactivated catalyst, and also, the compound can be deuterated without reducing the multiple bond, which may occur when a catalyst is activated with H₂ or D₂ gas during the deuteration reaction (see examples 26-32 in table 3 on page 31, particularly example 32 compared with comparative examples 1 and 2 on page 32, lines 1-14, and page 33, lines 3-13 of the specification).

Kato discloses a method of deuterating methyl acrylate and methacrylate with heavy water (D₂O) or D₂O and deuterium (D₂) gas in the presence of a catalyst (see coln. 1, line 67 – coln. 2, line 16). Kato, however, is silent about an activation of the catalyst before the deuteration reaction is performed (pre-activated catalyst) as claim 1 recites. If D₂O alone is used as a deuterium source, the catalyst cannot be activated and the deuteration ratio similar to that obtained with the pre-activated catalyst cannot be obtained (see example 32 and comparative example 1 in table 3 on page 31, page 32, lines 1-6, and page 33, lines 9-13 of the specification). If a combination of D₂O and D₂ gas is used as the deuterium source, the catalyst would be activated but the carbon-carbon double bond would be reduced with D₂ gas (see *id.* at comparative example 2 on page 32, lines 8-14 and page 33, lines 3-8). From Kato's disclosure, the high deuteration ratio such as 90 % that the method of claim 1 can provide cannot be expected (see *id.* at example 32 in table 3 on page 31, page 32, lines 1-14, and page 33, lines 3-13). Thus, claim 1 is distinguished from Kato.

Sajiki discloses a deuteration reaction of diphenylmethane with D₂O (see table 1 on page 1149). The compound of Sajiki, however, does not include a carbon-carbon multiple bond in an aliphatic portion of the compound as claim 1 recites. Generally, a double bond in an aromatic ring, i.e., a covalent bond in diphenylmethane, is more stable than a multiple bond in an aliphatic portion, and in Sajiki, protecting the double bond in the benzene rings would not be an issue when the hydrogen atoms outside the benzene ring in diphenylmethane are subject to the deuteration. In contrast, the compound deuterated by the method of claim 1 has at least one carbon-carbon multiple bond. The compound deuterated in Kato, i.e., methyl acrylate and methacrylate, having a carbon-carbon double bond in an aliphatic portion is completely different from the compound of Sajiki. Because the deuterated compounds are completely different from each other, there is no reasonable basis to assume that one method applicable to the particular first

group of compounds can provide similar results when applied to a second group of compounds that have a different structure and would have a different reactivity. Thus, there is no reason to combine the deuteration conditions of Sajiki with those of Kato.

Similar to Sajiki, Garnett I discloses deuteration of monohalogenated benzene and naphthalene, which do not have a carbon-carbon double bond or triple bond in an aliphatic portion recited in claim 1 (see abstract). The study of Garnett I is directed to finding a mechanism of the deuteration reaction of monohalogenated benzene and naphthalene, and Garnett I postulates that chemisorption of aromatic molecules on an active catalyst would occur through π -complex formation and that the chemisorption would be influenced with a size of the substituting halogen atom (see abstract). Methyl acrylate or methacrylate used in Kato's reaction has neither a halogen atom nor π -conjugated double bond system (see coln. 1, line 67 – coln. 2, line 16 of Kato), which can be formed in an aromatic ring or polydiene having a double bond and single bond alternately. Since the compounds of Kato are different from those of Garnett I and could not provide the chemisorption that Garnett I suggests, there is no reasonable basis to combine Garnett I with Kato.

In addition, diphenylmethane of Sajiki does not include a halogen atom, and the carbon atom having a hydrogen atom to be deuterated is not included in the π -conjugated double bond system as in monohalogenated benzene or naphthalene of Garnett I (see table 1 on page 1149 of Sajiki and figures on page 446 in Garnett I). Accordingly, there is also no reason to combine the deuteration method of Garnett I with that of Sajiki.

Similar to Garnett I, Garnett II is directed to deuteration of benzene, which has an aromatic ring forming the π -conjugated double bond system and does not have the carbon-carbon double bond or triple bond in an aliphatic portion as recited in claim 1 (see abstract and first para. under "Experimental" section on page 340 of Garnet II). Garnett II studies the mechanism of the deuterium exchange reactions from hydrogen to deuterium attaching to a carbon in the benzene ring (see first para. under "Introduction" section on page 339). As discussed above, there is no reasonable basis to assume that the deuteration reaction of hydrogen atoms in benzene of Garnett II would be similar to the deuteration of hydrogen atoms in an aliphatic portion including at least one multiple bond. Accordingly, similar to Garnett I, there also is no reasonable basis to combine

Garnett II with Kato or with Sajiki, both of which disclose deuteration of a compound(s) having no π -conjugated system at the deuterated portion to be deuterated (see coln. 1, line 67 – coln. 2, line 16 of Kato and table 1 on page 1149 of Sajiki).

Kawai discloses a polymer of tricyclo[5.2.1.0^{2,6}]deca-8-yl acrylate or methacrylate. The tricyclodecan portion of tricyclo[5.2.1.0^{2,6}]deca-8-yl acrylate or methacrylate monomer has no aromatic ring or polydiene, i.e., π -conjugated double bond system (see abstract and formula in coln. 1). Thus, there is no reasonable basis to combine Kawai with Garnett I or Garnet II.

In addition, the polymerization reaction as disclosed in Kawai is completely different from a deuteration reaction as disclosed in Kato. It is clear from Kato, in which oxygen is added to the deuteration system in order to inhibit the polymerization reaction (see coln. 2, lines 18-25 of Kato). Even if Kawai and Kato were combined for deuteration of Kawai's monomer compound, which Applicants do not concede, Kato is silent about the activation of the catalyst before performing the deuteration reaction that claim 1 recites. Since Kawai's tricyclo[5.2.1.0^{2,6}]deca-8-yl acrylate or methacrylate monomer (see formula in coln. 1) has a carbon-carbon double bond in the acrylate or methacrylate portion, the double bond can be reduced if D₂ is used as a deuterium source together with D₂O as Kato discloses (see coln. 2, lines 5-9 of Kato). Alternatively, if D₂O alone is used as the deuterium source as Kato discloses (see *id.*), a deuteration ratio would be significantly lower than that obtained by the method of claim 1 in which the catalyst is activated before the deuteration reaction is performed, as discussed for Kato above (see example 32 in table 3 on page 31, page 32, lines 1-14, and page 33, lines 3-13 of the specification). Thus, the combination of Kato and Kawai does not teach the deuteration method of claim 1.

Diphenylmethane deuterated in Sajiki does not have a carbon-carbon double bond in an aliphatic portion but has two benzene rings (see table 1 on page 1149), and Diphenylmethane is completely different from tricyclo[5.2.1.0^{2,6}] deca-8-yl acrylate or methacrylate monomer of Kawai. Therefore, there is no reason to combine Kawai with Sajiki.

Accordingly, claim 1, and claims 2-3, 5-6, 8-9, 13-14, and 16-17 that ultimately depend from claim 1 are distinguished from Kato in view of Sajiki, in further in view of Garnett I, in further in view of Garnett II, and in further in view of Kawai.

Claim 11 is directed to a method for deuteration of tricyclo[5.2.1.0^{2,6}]decan-8-ol. The claim recites a step of reacting tricyclo[5.2.1.0^{2,6}]decan-8-ol under neutral condition with a deuterated solvent other than D₂O₂ in the co-presence of palladium carbon as only activated catalyst.

As discussed for claim 1 above, there is no reasonable basis to combine Kato with Sajiki, Garnett I, Garnett II, or Kawai.

Further, the compounds to be deuterated in the references, such as methyl acrylate or methacrylate of Kato (see abstract and a formula in coln. 1), diphenylmethane of Sajiki (see table 1 on page 1149), monohalogenated benzene and naphthalene of Garnett I (see abstract), and benzene of Garnett II (see abstract), have a double bond(s) either in an aliphatic portion or in a benzene ring and do not include an alicyclic structure, particularly tricyclic structure as tricyclo[5.2.1.0^{2,6}]decan-8-ol of claim 11. Even among alicyclic compounds having no carbon-carbon double bond, the deuteration ratios vary when a number of carbon atoms, structures of the compounds, and substituents thereof differ from each other (see examples 6, 8, 14-25 in table 1-2 on pages 29-30 of the specification). Thus, there is no reasonable basis to assume that the compounds of Kato, Sajiki, Garnett I, and Garnett II can be deuterated similarly to each other and similarly to tricyclo[5.2.1.0^{2,6}]decan-8-ol of claim 11.

Moreover, even though Kawai's compound includes a tricyclic aliphatic structure, the compound does not include a hydroxyl group at the 8th position of the tricyclic structure and has an acrylate or methacrylate bound to the tricyclodecan portion through an ester bond (see abstract and formula in coln. 1). Thus, there is no reasonable basis to assume that tricyclo[5.2.1.0^{2,6}]decan-8-ol of claim 11 can be deuterated similarly to tricyclo[5.2.1.0^{2,6}]deca-8-yl acrylate or methacrylate of Kawai. Further, Kawai, which discloses polymerization of the tricyclo[5.2.1.0^{2,6}]deca-8-yl acrylate or methacrylate monomer (see abstract) is silent about deuteration of the tricyclo[5.2.1.0^{2,6}]deca-8-yl acrylate or methacrylate.

Accordingly, claim 11 is distinguished from Kato in view of Sajiki, in further in view of Garnett I, in further in view of Garnett II, and in further in view of Kawai.

Claims 12 and 15 also recite a method for deuteration of tricyclo[5.2.1.0^{2,6}] decan-8-ol. For at least the same reasons as discussed for claim 11 above, claims 12 and 15 are distinguished from Kato in view of Sajiki, in further in view of Garnett I, in further in view of Garnett II, and in further in view of Kawai. Accordingly, this rejection should be withdrawn.

In view of the above, Applicants request reconsideration of the application in the form of a Notice of Allowance.



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